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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/961,128 | 09/21/2001 | Marianne Kearney | 49138 (71417) | 4197 |

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EXAMINER

QIAN, CELINE X

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1636

10

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/961,128

Applicant(s)

KEARNEY ET AL.

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 4,5,13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,6-12 and 15-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 September 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-17 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group II in Paper No. 9 is acknowledged. The traversal is on the ground(s) that a search of Groups II, III and IV would not pose undue burden. This is not found persuasive because the inventions of Groups I-IV are considered as patentably distinct species. A search of one group would not be co-extensive with a search of another group. A search of all four groups in a single application is burdensome.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 4, 5, 13 and 14 are withdrawn from consideration for being directed to non-elected subject matter. Claims 1-3, 6-12 and 15-17 are currently under examination.

Drawings

Figure 1 comprises 1A-1C. The drawings are objected to because the drawing description only describes Figure 1 but fail to acknowledge each individual drawing. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

Claims 1-3, 6-12 and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 1-3, 6-12 and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

See MPEP § 2172.01. The omitted steps are: how to determine the ability of the plasmid encoding an endothelial cell mitogen to produce a biologically active endothelial mitogen protein or how to determine the ability of the first or second plasmid encoding an endothelial cell mitogen to produce a biologically active endothelial mitogen protein. In other words, the method steps must refer back to the preamble.

Regarding claims 10-12 and 15-17, the recitation of "with plasmid containing a gene encoding for an endothelial cell mitogen" on line 12 of claim 10 renders the claims indefinite because it is unclear which plasmid it is referring to. In other words, is it the first plasmid construct or the second? Similarly, the recitation of the term "the plasmid" in claim 11 and 12 also renders the claims indefinite, because it is unclear which plasmid it is referring to.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 7-12, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sugihara et al., in view of Buttke et al (Journal of Immunological Methods, 1993, Vol 157, p.233-240).

Sugihara et al. teach a method for testing the biological activity of VEGF115 and VEGF164 comprising a) transiently transfecting NIH 3T3 cells with a vector encoding VEGF; b) incubating HUVEC cells with conditioned media from the NIH 3T3 cells transfected with VEGFs or control vector; c) determining the cell survival by thymidine incorporation (see page 3037, 2nd col., 3rd paragraph). Sugihara et al. further teach that the level of cell survival of HUVEC cells treated with conditioned media from either VEGF115 or VEGF164 is significantly higher (more than 25% fold) than that of the control cells (see Figure 5B). However, Sugihara et al. do not teach measuring cell survival by tetrazolium (MTS)/formazan assay.

Buttke et al. teach a method of measuring cell survival by using an MTS/formazan assay. Buttke et al. teach that MTS can be reduced by living cells to yield a formazan product that can be assayed colorimetrically (see abstract). Buttke et al. further indicate that this method has the advantage of producing soluble formazan that eliminates the need of using detergent or organic solvent for extraction, rapid color development and storage stability (see abstract).

It would have been obvious to one of ordinary skill of art to develop a method of testing the biological activity of a endothelial cell mitogen protein such as VEGF by measuring the survival rate of endothelial cells incubating with conditioned media collected from host cells

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transfected with vector encoding a endothelial cell mitogen based on the teaching of Sugihara et al. Methods of measuring cell survival are well known in the art. Such method includes MTS/formazan assay taught by Buttke et al. One of ordinary skill in the art would have been motivated to use MTS/formazan assay because its advantage over other assay including rapid color development, storage stability and elimination of the use of detergent or organic solvent extraction step. The level of skill in the art is high. Absent evidence from the contrary, one of ordinary skill in the art would have reasonable expectation of success to practice the method as claimed. Therefore, the invention is *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

Claims 6 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sugihara et al., in view of Buttke et al. and Delli-Bovi et al.

The teachings of Sugihara et al and Buttke et al. are discussed above. However, Sugihara et al. do not teach using Cos-1 cell line as host cells expressing the endothelial mitogen protein.

Delli-Bovi et al. teach a method of testing whether the K-FGF protein would promote the NIH3T3 cells in conditioned medium from host cells transfected with vector expressing K-FGF (see page 2938, 1st paragraph, lines 1-7). Delli-Bovi et al. teach that the conditioned medium collected from Cos-1 cells transfected with plasmid expressing K-FGF and added to the growth medium of NIH3T3, and the cell number is measured subsequently (see Figure 6).

It would have been obvious to one of ordinary skill of art to used the method taught by Sugihara et al. and using Cos-1 cell as host cell for expressing endothelial cell mitogen protein because both NIH3T3 cells and Cos-1 cells are widely used in transfection experiment and expressing a protein of interest. The ordinary artisan would have been motivated to use either

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Cos-1 or NIH3T3 as host cells because both Sugihara et al. and Delli-Bovi et al. teach that conditioned media from either cell line transfected with endothelial mitogen protein promotes endothelial cell growth. The level of skill in the art is high. Absent evidence to the contrary, one of ordinary skill in the art would have reasonable expectation of success to use Cos-1 cells to express a biological active endothelial mitogen protein. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
July 25, 2003

Anne-Marie Falk
ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER